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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/037,460	03/10/98	HASTINGS G	325800-626(P

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EXAMINER	
SAOUD, C	
ART UNIT	**PAPER NUMBER**
1647	24

DATE MAILED: 12/15/00

Please find below and/or attached an Office communication concerning this application or pr ce ding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/037,460	Applicant(s) HASTINGS et al.
	Examiner Christine Saoud	Group Art Unit 1647

☒ Responsive to communication(s) filed on *Oct 25, 2000* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *54-67, 75-92, 102-107, 115-119, and 122-175* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *54-67, 75-92, 102-107, 115-119, and 122-175* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *22*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. Claims 120 and 121 have been canceled and claim 15 has been amended as requested in the amendment of paper #23, filed 25 October 2000. Claims 54-67, 75-92, 102-107, 115-119, and 122-175 are pending in the instant application.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed 25 October 2000 have been fully considered but they are not deemed to be persuasive.

Claim Rejections - 35 USC § 101

5. Claims 54-67, 75-92, 102-107, 115-119 and 122-175 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for the reasons of record in paper #20. The instant application has

provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance.

Applicant argues that "sequence relatedness or homology has, and is being used by those of skill in the art to predict function based on sequence" and cites Dunwell et al. in support of this position. However, a fair reading of Dunwell et al. does not lead to the conclusion that function can be predicted from structure. Even the title of Dunwell, "Microbial Relatives of the Seed Storage Proteins of Higher Plants: Conservation of Structure and Diversification of Function during Evolution ..." suggests that conservation of structure is not predictive of function. The rejection of the instant claims was premised on the fact that proteins which are members of the CCN protein family share common amino acid sequence identity, but do not share common biological functions, therefore, one of ordinary skill in the art would not be able to predict which biological function would be possessed by a protein with a similar amino acid sequence. As stated by Dunwell, "simple analysis of primary sequence provides no information about the secondary or tertiary structure of the protein(s) under investigation, and it is the structure of a protein that determines its function" (see introduction). Therefore, Applicant's statement that "prediction of VIGF activity based on a shared percent identity of 40-45% with the CCN family in the instant specification would be found credible by those skilled in the art" has no basis in fact when Dunwell expressly states that primary sequence provides no information as to "structure" which determines its function. Applicant cites Wilson et al. for stating that "40% sequence identity corresponds to a sharing of precise function while sequence identities of about 25% comprise a

functional class". However, a fair reading of Wilson indicates that this is true of enzymes, and that this is not necessarily the case with nonenzymes in that "[t]here are differences between the functional conservation thresholds of enzymes and non-enzymes, with enzymes appearing to more highly conserve precise function than nonenzymes, but nonenzymes conserving functional class more highly than enzymes". With this in mind in view of Dunwell, one of ordinary skill in the art would not reasonably conclude *which* biological function would be possessed by the claimed invention, as it appears to be a member of a family of proteins which have distinct and diverse biological functions, absent evidence to the contrary.

Applicant argues at page 4 of the response that Lassale et al. confirmed VIGF as having endothelial and smooth muscle cell specific expression and that they also predict that VIGF participates in vascular cell biology and human lung physiology. This point is noted, however, it still does not provide a specific, substantial and credible utility for the claimed invention. Expression of the claimed polynucleotide in endothelial and smooth muscle cells does not equate to a specific, substantial and credible utility. The likelihood that the claimed polynucleotide encodes an inhibitor of vascular smooth muscle and endothelial cell proliferation is just as great as that it encodes a stimulator of proliferation. Additionally, the claimed polynucleotide may be specific for one cell type versus another, which cannot be predicted from its pattern of tissue expression. At present, the instant claims are drawn to a nucleic acid which encodes a protein of as yet undetermined function or biological significance. The statement of Lassalle that "ESM-1 may have potent implications in the areas of vascular cell biology and human lung physiology"

does not provide a function or biological significance to the claimed invention. A number of proteins are important for vascular cell biology and lung physiology, however, without knowing the biological activity or significance of these proteins, one of ordinary skill in the art would not know how to use them in any meaningful manner, absent evidence to the contrary.

Applicant argues that the Examiner bears the burden of proof in order to demonstrate that the claimed invention lacks the asserted utility. However, "detailed explanation why the claimed invention has no specific and substantial credible utility" was provided in the previous Office action. Applicant appears to be asserting that it is the responsibility of the Examiner to prove that the claimed invention is without utility. The Examiner is under no obligation to prove a negative, the Examiner must simply provide sound reasoning in support of a conclusion that an element is lacking from a specification, and this has been done. Applicant argues that the Examiner's contention is not supported by the relevant art and that the cited references support the conclusion that "VIGF can be used, for example, to enhance the growth of vascular smooth muscle and endothelial cells leading to the stimulation of angiogenesis" (see page 5 of the response). However, this conclusion is not supported by any evidence of record. The references which were cited fail to teach that the claimed invention enhances the growth of vascular smooth muscle or endothelial cells, therefore, this utility is not credible. The cited references fail to teach that the amino acid sequence of the disclosed protein will provide for the function of enhancing the growth of vascular smooth muscle or endothelial cells, and reasons as to why one of ordinary skill in the art would not conclude that this activity would be possessed by the claimed invention

have been provided. This situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The instant specification provides no evidence supporting the claimed utility in that tissue expression patterns and amino acid sequence similarity are not sufficient evidence to conclude that the claimed invention could be used in the manner disclosed in the instant specification. Additionally, the family of proteins to which the claimed invention is alleged to belong have divergent biological activities, therefore, even if the nucleic acid encodes a protein of the CCN family, one of ordinary skill in the art could not use the claimed invention in a real world manner because one cannot predict which biological activity which are associated with the protein family will be possessed by the claimed invention. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the vascular IBP-like growth factor (VIGF) of the instant application can be used for wound healing and associated therapies, for enhancement of growth of vascular smooth muscle and endothelial cells, and therapeutically in ischemic tissues and for coronary stenosis (see page 19 of the specification) for the reasons provided above.

6. Claims 54-67, 75-92, 102-107, and 115-119, and 122-175 are rejected under 35 U.S.C. §112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. §101.

Applicant argues that the claimed nucleic acids have specific and substantial uses "to enhance the growth of vascular smooth muscle and endothelial cells leading to the stimulation of angiogenesis". This argument is not persuasive because there is no evidence of record that the claimed nucleic acids encode a protein with this biological activity, therefore, the disclosed utility is not credible. The claimed invention shares sequence identity to members of the CCN family, wherein the biological activities of the family members is divergent, including members which have stimulatory activity and members which have inhibitory activity. There is no evidence of record to support the disclosed utility, therefore, the disclosed utility is not credible. As in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), a steroid which was structurally similar to other steroids, some of which had anti-tumor activity, was found to lack utility in the absence of evidence that the particular steroid of the claims had anti-tumor activity.

It is again noted that the claims are also directed to nucleic acid molecules comprising contiguous portions of SEQ ID NO:1. These claims encompass genomic DNA, for which the instant specification fails to provide a written description. Therefore, these claims are also directed subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant did not appear to traverse this ground of rejection, therefore, the rejection is being reiterated and maintained at this time.

Conclusion

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 14, 2000

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud